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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,712	11/24/2003	Kenji Sugimoto	245901US0	9928

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,712	SUGIMOTO ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2005 and 12 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-44* is/are pending in the application.

4a) Of the above claim(s) *31-38,43 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30 and 39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix I*.

DETAILED ACTION

This action is in response to the amendment, filed 8/30/2005, in which claims 1-20 were canceled; and claims 21-44 were newly added. Applicants' arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicants elected Group I (claims 1-10), and histone H3 (chromosome) and importin α (nuclear membrane) species with traverse in the reply filed on 1/28/2005.

Claims 43 and 44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable product claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/28/2005.

New claim 21 requires at least three fusion proteins, wherein at least one fusion protein comprises a spindle polypeptide. Applicants elected histone H3, a nucleus/chromosomal polypeptide, and importin α, a nuclear envelope polypeptide, in the reply filed on 1/28/2005.

Claims 31-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/28/2005.

Currently, claims 21-30 and 39-42 are under consideration.

Claim Rejections - 35 USC § 112

Claims 29, 39 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection, necessitated by the amendment of the claims, filed 8/30/2005, to add new claims 29, 39 and 40.

Claim 29 is vague and indefinite in that the metes and bounds of the term "centrosome/spindle polypeptide" are unclear. It is unclear if the polypeptide must localize to the centrosome and spindle or if the polypeptide must localize to either the centrosome or spindle. Thus the boundaries of the genus of polypeptides encompassed by the term are unclear.

Claims 39 and 40 are vague and indefinite in that the metes and bounds of the term "nucleus/chromosomal polypeptide" are unclear. It is unclear if the polypeptide must localize to the nucleoplasm and chromosome or if the polypeptide must localize to either the nucleoplasm or chromosome.

Response to Arguments - 35 USC § 112

The previous rejection of claims 2-4 and 8-10 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims, filed 8/30/2005.

Claim Rejections - 35 USC § 102

Claims 21-30 and 39-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugimoto et al (Molecular Biology of the Cell, Vol. 13, pages 50a-51a, Abstract 282, November 1, 2002, cited in a prior action; see the entire abstract). This rejection was set forth in the previous action and has been altered to address the new claims, filed 8/30/2005.

Sugimoto et al teach a mammalian cell line comprising three fusion genes: histone H3 fused to cyan fluorescent protein (CFP-histone H3), importin α fused to red fluorescent protein (DsRed-importinα), and Aurora-A fused to green fluorescent protein (GFP-Aurora-A) (paragraph bridging pages 50a-51a). CFP-histone H3, DsRed-importinα, and EGFP-Aurora-A localize to the following cell structures: chromosome, nuclear membrane, and centrosome, respectively (paragraph bridging pages 50a-51a).

Regarding claim 42, the human cell taught by Sugimoto et al must be a somatic cell or germ cell, because the human body is composed of somatic cells and germ cells.

Claims 21-23, 25, 27-29, 39, 41 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001, cited in a prior action; see the entire reference) as evidenced by Oakley et al (Cell Structure and Function, Vol. 24, pages 365-372, 1999; see the entire reference). This is a new rejection, necessitated by the amendment of the claims, filed 12/12/05, to include new claims drawn to a cell that has been transformed with a polynucleotide encoding a fusion protein comprising a spindle polypeptide.

Gerlich et al teach NRK cells (i.e. mammalian somatic cells) comprising three fusion genes: histone H2B fused to cyan fluorescent protein (H2B-CFP), lamin B receptor fused to green fluorescent protein (LBR-GFP), and γ-tubulin fused to red fluorescent protein (γtubulin-RFP) (e.g. page 855, Cells and DNA constructs; Figure 2). H2B-CFP, LBR-GFP, and γtubulin-RFP localize to the following cell structures: chromosome, nuclear membrane, and centrosomes, respectively (e.g. page 853, right column; Figure 2). Furthermore, Gerlich et al teach the use of

the cell to study cell division during late anaphase (e.g. page 853, right column, first full paragraph).

Oakley et al is cited merely to provide evidence that γ-tubulin localizes to the spindle in addition to the centrosome (e.g. page 367, Cellular location of γ-tubulin).

Therefore, the teachings of Gerlich et al meet each of the claim limitations recited in each of the rejected claims.

Response to Arguments - 35 USC § 102

Applicant's arguments filed 8/30/2005 have been fully considered but they are not persuasive. The response asserts that Sugimoto et al, Mol. Biol. Cell 13:50a-51a was not publicly available prior to the present application's filing date (November 24, 2002). The response provides evidence that the paper copy of the abstract was not mailed until after November 24, 2002. Thus, the response asserts that the reference is not applicable under 35 USC 102(b) and should have been applied under 35 USC 102(a).

The response is not persuasive because the abstract was publicly available online prior to November 24, 2002. The publisher has indicated that the abstract was available online October 7, 2002 (see Appendix I). Therefore, the abstract was publicly available prior to November 24, 2002 and was properly applied under 35 USC 102(b). The declaration under 37 CFR 1.132, stating that the cited reference is not the work of another, cannot be used to overcome this statutory bar.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Applicant's arguments filed 8/30/2005 have been fully considered but they are not persuasive. The response asserts that Gerlich does not disclose cells transformed with fusion proteins containing a spindle polypeptide. The response asserts that γ-tubulin is a centrosome polypeptide and is not a spindle polypeptide. Further, the response asserts that using the Gerlich cells it is not possible to observe the dynamic state of the spindle during the mitotic period.

The response is not found persuasive because the γ-tubulin protein is a spindle protein in addition to a centrosome protein (see the teachings of Oakley et al discussed above). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., observation of the dynamic state of the spindle during the mitotic period) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims require that the fusion proteins are expressed at a level sufficient to permit their visualization during cell division. Gerlich et al teaches sufficient expression of the nucleic acids encoding the spindle polypeptide, chromosome and nuclear membrane fusion proteins in order to visualize the proteins during cell division (e.g. Figure 2b).

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Response to Amendment - 35 USC § 102

The declaration under 37 CFR 1.132 filed 8/30/2005 is sufficient to overcome the rejection of claims 1-10 based upon the Sugimoto et al reference (Cell Structure and Function, Vol. 27, pages 457-467, December 1, 2002; see the entire reference) applied under 35 U.S.C. § 102(a).

The Sugimoto et al (Molecular Biology of the Cell, Vol. 13, pages 50a-51a, Abstract 282, November 1, 2002) reference is a statutory bar under 35 U.S.C. 102(b) and thus has not been overcome by the declaration under 37 CFR 1.132.

Claim Rejections - 35 USC § 103

Claims 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlich et al (Nature Cell Biology, Vol. 3, pages 852-855, 2001, cited in a prior action; see the entire reference) in view of Kimura et al (The Journal of Cell Biology, Vol. 153, No. 7, pages 1341-1353, 2001, cited in a prior action; see the entire reference) further in view of Kim et al (The Journal of Biological Chemistry, Vol. 275, No. 30, pages 23139-23145, 2000, cited in a prior action; see the entire reference), as evidenced by Oakley et al (Cell Structure and Function, Vol. 24, pages 365-372, 1999; see the entire reference). This is a new rejection, necessitated by the amendment of the claims, filed 12/12/05, to include new claims drawn to a cell that has been transformed with a polynucleotide encoding a fusion protein comprising a spindle polypeptide. The teachings of Gerlich et al are described above and applied as before.

Gerlich et al do not teach a cell comprising the fusion genes encoding the following fusion proteins: (i) histone H3 fused to a fluorescent protein, and (ii) importin α fused to a fluorescent protein.

Oakley et al is cited merely to provide evidence that γ-tubulin localizes to the spindle in addition to the centrosome (e.g. page 367, Cellular location of γ-tubulin).

Kimura et al teach the replacement of histone H2B coding sequence, in a plasmid encoding a histone H2B-green fluorescent protein fusion protein, with histone H3 coding sequence such that a histone H3-green fluorescent protein (H3-GFP) fusion gene is made (e.g. page 1342, Plasmid Construction, Transfection, and Cell Fusion). Further, Kimura et al teach the transfection of the H3-GFP fusion gene into mammalian somatic cells (e.g. page 1342, Plasmid Construction, Transfection, and Cell Fusion). Moreover, Kimura et al teach that histone H3 is more stably integrated into chromatin as compared to histone H2B in that greater than 80% of histone H3 remains bound permanently to the chromosomes whereas about 53% of histone H2B remains bound permanently (e.g. Figure 7, pages 1351-1352, Transcriptional Activity of the Different Population, Concluding Remarks).

Kim et al teach the fusion gene comprising importin α and green fluorescent protein (GFP) coding sequences (e.g. page 23140, Plasmid Construction and Expression of Fusion Proteins). Further, Kim et al teach the transfection of mammalian somatic CHO-K1 cells, where the Importin α-GFP fusion protein localized to the nucleus (e.g. Figure 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising fusion genes of Gerlich et al to replace the H2B coding sequence in the H2B-CFP construct taught by Gerlich et al with the H3 sequence of Kimura et al

because Gerlich et al teach the use of H2B coding sequence to monitor chromosomes and Kimura et al teach the localization of histone H3-GFP to chromosomes. Further, Kimura et al specifically teach the replacement of the H2B coding sequence with H3 coding sequence within a fusion protein gene comprising a fluorescent protein. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the cell comprising fusion genes of Gerlich et al to include the importin α fusion gene in addition to the fusion genes taught by Gerlich or as a replacement of the coding sequence in the γtubulin-RFP construct because Gerlich et al teach it is within the skill of the art to make cells comprising fluorescent fusion proteins to monitor cell division and Kim et al teach the localization of Importin α-GFP to the nucleus, a cellular structure involved in cell division.

One would have been motivated to make such a modification to include a histone H3-fluorescent protein construct in order to receive the expected benefit of more stable integration of histone H3 into chromosomes as compared to histone H2B as taught by Kimura et al. Further, one would have been motivated to include an importin α-fluorescent protein construct to receive the expected benefit of being able to monitor the nucleus of the cell as taught by Kim et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

Applicant's arguments filed 8/30/2005 have been fully considered but they are not persuasive. The reference asserts that Gerlich does not teach the present invention, which

involves a spindle polypeptide. Further, the response asserts that the Kimura and Kim references do not cure this deficiency. As discussed above, Gerlich teaches a cell comprising a polynucleotide encoding a protein comprising a spindle protein (γ-tubulin). Thus, the combined teachings of the references meet each of the limitations of the rejected claims.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Jennifer Dunston
Examiner
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